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Applicants: Robert E. Canfield, et al.

Serial No.: 09/404,076

Examiner: P.J. Nolan

Filed : September 23, 1999
(CPA filed herewith)

Group Art Unit: 1644

For : ANTIBODIES SPECIFIC FOR HLH BETA CORE FFAGMENT AND
USES THEREOF

1115 Avenue of the Americas
New York, NY 10036
May 10, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231
BOX CPA

Sir:

**PRELIMINARY COMMUNICATION
AND REQUEST FOR A THREE-MONTH EXTENSION OF TIME**

This Preliminary Communication is submitted in connection with a December 21, 2001 Advisory Action and in order to address the Examiner's rejections made in the June 4, 2001 Final Office Action issued in connection with the above-identified application. The December 21, 2001 Advisory Action states that applicants' proposed Amendment filed on December 4, 2001 was not entered. Applicants are filing Continuation Prosecution Application ("CPA") papers herewith, and hereby request that the Examiner enter the Amendment filed on December 4, 2001.

Applicants note that on December 4, 2001, a petition for a three-month extension of time and a Notice of Appeal were also filed. The Notice of Appeal was received by the Patent and Trademark Office on December 10, 2001, making an Appeal Brief originally due February 10, 2002, under M.P.E.P. §512. Applicants hereby petition for a three-month extension of time

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for filing an Appeal Brief. The fee for a three-month extension is FOUR HUNDRED AND SIXTY DOLLARS (\$460.00) for a small entity, and applicants have previously established small entity status. A check for \$830.00 is enclosed herewith, which amount includes the \$460.00 extension fee and the \$370.00 filing fee for a CPA. Thus, this application is pending until today, May 10, 2002, and the accompanying CPA papers are being timely filed.

REMARKS

Claims 1 and 4 are pending. No claims have been added, canceled or amended herein. Thus, claims 1 and 4 are still pending and under examination.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the June 4, 2001 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 1 and 4 under 35 U.S.C. §103(a) as allegedly unpatentable over O'Connor et al. (1994) and further in view of Campbell (1984).

In response to the Examiner's rejection, applicants respectfully traverse for the reasons given in their December 4, 2001 Amendment, and for the additional reasons set forth below.

The present invention is based upon the surprising discovery of antibodies that specifically bind to urinary hLH β core fragment without cross-reacting with other antigenically similar urinary proteins. Specifically, claim 1 provides an antibody which binds to the hLH β core fragment without cross-reacting with the hLH, hLH β or hCG β core fragment molecules present in urine. Claim 4 provides antibodies which

competitively inhibit the binding of the antibody of claim 1 to the hLH β core fragment.

In asserting that the claimed antibodies are obvious over O'Connor and Campbell, the Examiner ignores applicants' unexpected discovery and, in doing so, engages in hindsight.

Specifically, O'Connor teaches the chemistry and immunochemistry of human chorionic gonadotropin (hCG) and the impact thereof on clinical measurements of hCG. Campbell teaches the art of monoclonal antibody production generally, but does not consider at all the well-known difficulties in generating antibodies specific to particular gonadotropins and their metabolites.

Notably, O'Connor does not teach or suggest any antibodies against hLH molecules. While conceding this point, the Examiner nonetheless argues that the discovery of a pituitary hLH β core fragment molecule in 1993, as taught by O'Connor, provides both sufficient motivation and a reasonable expectation of success for one of skill to produce the antibodies of the instant invention.

Contrary to the Examiner's assertion, knowledge of a pituitary hLH β core fragment molecule does not render the claimed antibodies obvious, given the absence of sufficient information at the time regarding the hLH β core fragment molecule. First, it was unknown at the time of this invention whether the hLH β core fragment was present in tissues or fluids other than the pituitary, such as urine. Second, it was unknown whether hLH β core fragment, if present in urine, would share the same antigenic determinants as its pituitary counterpart. Third, given the presence of immunologically similar molecules in the urine, it was unknown whether it would be possible to produce antibodies with the required binding specificity to accurately measure a urinary hLH β core fragment. Given this level of uncertainty, one of ordinary

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skill at the time of this invention would have had no motive to combine the cited references and no reasonable expectation of successfully producing the instant antibodies.

In support of their position, applicants direct the Examiner's attention to page 654, column 2, paragraph 3, of O'Connor. There, O'Connor teaches that a material present in urine was known to exhibit cross-reactivity with the hCG β core fragment. O'Connor fails to state with any certainty whether this urinary material was of hCG or hLH origin. Applicants maintain that, in view of such confusion as to the nature of the urinary material, the mere disclosure of a pituitary hLH β core fragment molecule, absent any other motivating factors present in either O'Connor or Campbell, would not have provided sufficient motivation to make the instant antibodies.

Applicants further maintain that, contrary to the Examiner's assertion, there was no reasonable expectation that the instant antibodies could even be produced. In support of this point, applicants again stress the uncertainty in the art regarding the existence and antigenic features of a urinary hLH β core fragment molecule. Furthermore, it would not have been predictable that an antibody specific to a pituitary form of the molecule would also bind with the same specificity to a urinary form if it did exist.

This lack of predictability is clear from the fact that the urinary forms of gonadotropin hormones are subject to additional proteolytic degradation in peripheral circulation compared with their counterparts isolated from tissue. Thus, one could reasonably expect the urinary and tissue forms of the molecules to present different antigenic determinants. This fact alone, apart from the well-documented difficulties in obtaining specific antibodies for the urinary species of gonadotropins, would have precluded a reasonable expectation of success in generating the instant antibodies, since one could not assume that the same antigenic determinants would be

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present on both the pituitary and urinary forms of the molecule. Campbell does nothing to overcome these deficiencies of O'Connor. Accordingly, applicants maintain that O'Connor and Campbell, taken together, do not render the claimed invention obvious.

In view of the above remarks, applicants maintain that claims 1 and 4 satisfy the requirements of 35 U.S.C. §103.


Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed extension and CPA fee, is deemed necessary in connection with the filing of this Preliminary Communication. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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